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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/851,743	05/09/2001	James Nolan	00-388-A	4067

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EXAMINER	
SHARAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 04/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/851,743	NOLAN ET AL.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,6-16,18-26,28-31 and 33-35* is/are pending in the application.

4a) Of the above claim(s) *8-12 and 20-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-7, 13-16, 18-19, 25-26, 28-31, 33-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment filed on January 12, 2006 has been entered. Claims 1-4, 6-16, 18-26, 28-31, 33-35 are pending. Claims 8-12, 20-24 stand withdrawn for the reasons of record. Applicant's arguments with respect to claim 1-4, 6-7, 13-16, 18-19, 25-26, 28-31, 33-35 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-4, 6-7, 13-16, 18-19, 25-26, 28-31, 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banknieder et al US Patent 4,751,243 in view of York US Patent 4,600,717 and DiPiro et al Pharmacotherapy, A Pathophysiologic Approach, 2nd ed. Elsevier Pub, pp. 41-46.

The scope of the instant claims is viewed given their broadest reasonable interpretation consistent with the specification. Accordingly, the claims are directed to methods of identifying a compound for treatment of wounds to dermis or epidermis of external body surface in a diabetic animal, which also includes ophthalmic wounds. The method comprises producing a wound at a site of interest, expose the wound topically to a alsdse reductase inhibitor, and assess the rate of wound healing. Claims 2 and 14 further require assessing the efficacy of another compound against the employed aldose reductase inhibitor.

Banknieder discloses methods of improving wound healing by administering an effective amount of tolerstat, which is an aldose reductase inhibitor compound to a

patient. (abstract). Bankneider discloses methods of identifying the efficacy of tolerstat as a compound for healing wounds in diabetic rats against controlled subjects. (see col 2, line 13-col 3, line 20). Bankneider created a wound in diabetic animal models, treated the animals with controls, regular diet and tolerstat doses and subsequently determined that rats that were treated with had improved wound healing (see entire col 2-3; claims 1-5). The wounds created by Bankneider is on the skin and thus on the dermis or epidermis of the subjects.The controls and regular diet of Bankneider's Group III meets the limitations of the instant claim 2 and 14 of comparing wounds in the presence of a test compound, because at least the instantly recited test compounds encompass the regular diet of Bankneider. Bankneider further claims methods of treating human with wounds from diabetes mellitus. Bankneider only fails to administer his aldose reductase inhibitor topically the epidermis or dermis wound and use punch biopsy to produce the wound.

York shows topical administration of aldose reductase inhibitors in suitable carrier system. York also shows effective treatment of ocular wounds in humans by administering various aldose reductase inhibitors also disclosed in his parent cases. (see abstract, col 1, lines 25-59; col 2, lines 1-67).

Depiro et al is merely used to show that it is well within the purview of one of ordinary skill in the art to prepare a topical or ophthalmic formulation, once in possession of the active ingredient. (see p 42-45, specifically sections under biopharmaceutical and therapeutic considerations). Accordingly, converting a ophthalmic to a topical composition is a matter of optimizing the carrier system.

Thus, it would have been also obvious to one of ordinary skill in the art at the time of invention to practice Banknieder's method by administering his aldose reductase inhibitor topically to a site of interest on the skin, because as shown by York, such compounds as aldose reductase inhibitors, can provide their wound healing properties when administered topically. The ordinary skill in the art would have had a reasonable expectation of success because, as described by York, aldose reuctase inhibitors provide their wound healing effects when administered topically.

In addition, absence of a showing unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention to treat a wound in respective studied subjects by any known mechanism of producing a wound, such as punch biopsy, because the ordinary skill in the art would have expected to see the same results in any type of skin wound created on the skin.

Claims 1-4, 6-7, 13-16, 18-19, 25-26, 28-31, 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over York US Patent 4,600,717 in view of FDA Guideline No. 38, Guideline For Effective Evaluation of Topial/Otic Animal Drugs, revised Aug 21, 1984, Center for Veterinary Medicine. 8/21/1984, available at. fda.gov/cvm/guidance/guidline38.htm. Last visited Sep 2005. ("Guideline No. 38"), Chen US Patent 6,232,341 and DiPiro et al Pharmacotherapy, A Pathophysiologic Approach, 2nd ed. Elsevier Pub, pp. 41-46

York shows topical administration of aldose reductase inhibitors in suitable carrier system. (abstract, col 2, lines 30-65). York also shows suggests effective treatment of ocular wounds in diabetic humans by administering various aldose

reductase inhibitors. (see abstract, col 1, lines 20-59; col 2, lines 1-67). York fails to compare the efficacy of his compositions against other potentially useful agents.

Guideline No. 38 is merely used to show the standard for assessing topical efficacy of candidate drugs. Attention is drawn to section VIII-X, wherein the study format and appropriate control groups are recommended by the FDA to substantiate the efficacy results of any give drug. (see specifically Sec IX).

Chen is used as an example of the Guideline No. 38 in a clinical efficacy study. Chen shows the state of art as to methods of assessing the efficacy of topical therapeutic preparation in treating skin wound comprising creating a wound, applying the drug of interest randomly among animals, comparing the rate of healing and assessing the efficacy of the drug (see example 3, col 5-8). Chen does not teach the use of his methodology on comparing the efficacy of topical agents against aldose reductase inhibitors in diabetic animals.

Depiro et al is merely used to show that it is well within the purview of one of ordinary skill in the art to prepare a topical or ophthalmic formulation, once in possession of the active ingredient. (see p 42-45, specifically sections under biopharmaceutical and therapeutic considerations). Accordingly, converting a ophthalmic to a topical composition is a matter of optimizing the carrier system.

Nevertheless, it would have been obvious to one of ordinary skill in the art at the time of invention, to use compare aldose reductase inhibitors of York against other potential candidate agents by as described by Guideline No. 38 and exemplified by Chen's methodologies, because as taught by the Guideline No. 38 and Chen, such

methods of comparative analysis is well practiced in the art for assessing the cutanaous effects of drugs on ulcer or burn wounds of dermis or epidermis. The ordinary artisan would have had a reasonable expectation in observing positive results comparative results against aldose reductase inhibitors because they are proven to be effective as a wound-healing agent.

Response to Arguments

Applicant's arguments filed January 12, 2006 have been fully considered but they are not persuasive.

First, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Here, the teachings of prior art is in view of the combined teaching of the reference as they meet all elemental components of the claims. Specifically, Banknieder and further Guideline No. 38 describe topical wounds on epidermis or dermis. Thus, all limitation of the claims are described by the combined teaching of the references.

Second, in response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir.

1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the knowledge generally available to one of ordinary skill in the art. In the art of pharmaceutical formulations, there is ample information available to one of ordinary skill in the art to prepare carrier systems that is suitable for topical application of compounds to skin or the eye. Accordingly, once a desired active agent is identified preparing a topical or ophthalmic formulation is well within the level of one of ordinary skill in the art. Thus, applicant's arguments are not persuasive.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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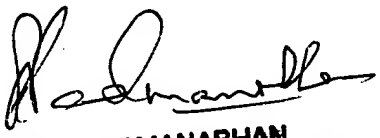

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER